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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/573,632

03/28/2006

Jeremy Richard Graff

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9016

25885 7590 05/01/2009

ELI LILLY & COMPANY

PATENT DIVISION

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EXAMINER

PACKARD, BENJAMIN J

ART UNIT

PAPER NUMBER

1612

NOTIFICATION DATE

DELIVERY MODE

05/01/2009

ELECTRONIC

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patents@lilly.com

<b>Office Action Summary</b>	<b>Application No.</b> 10/573,632	<b>Applicant(s)</b> GRAFF, JEREMY RICHARD	
	<b>Examiner</b> Benjamin Packard	<b>Art Unit</b> 1612	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 06 January 2009.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-20 is/are pending in the application.
- 4a) Of the above claim(s) 13-20 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-12 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)          | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

### **DETAILED ACTION**

Applicants' arguments, filed 1/06/09, have been fully considered. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

#### ***Claim Rejections - 35 USC § 112 - Indefiniteness***

**Claims 6 and 12** stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicants assert this rejection is moot with the cancellation of claims 6 and 12.

Examiner notes Applicants may have filed the wrong claim set as the claims filed 01/06/09 did not cancel claims 6 and 12. Because the claims were not properly cancelled, the rejection is maintained.

#### ***Claim Rejections - 35 USC § 103***

**Claims 1-12** stand rejected under 35 U.S.C. 103(a) as being unpatentable over Heath et al (US 5,668,152) in view of Comfort et al (AJP, Vol. 154, No. 1 (1999) 137-144).

Applicants assert the supporting declaration is sufficient to rebut an obviousness rejection, given the supporting data in the declaration shows the claimed compounds have superior activity in prostate cancer over structurally related compounds due to the

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dual mechanism discovered by Applicants. Additionally, Applicants suggest the Examiner misconstrues the evidence and does not recognize the increased effectiveness against specific tumor cell lines, regardless of mechanism involved.

Examiner believes the showing is not sufficient to overcome the rejection.

First, Applicant's compound is specifically disclosed in the prior art and specifically disclosed to have PKC inhibitory effect, which the secondary reference teaches can be used to treat androgen-independent prostate cancer. Therefore it would be expected that the compound would have an inhibitory effect on androgen-independent prostate cancer and prostate cancer generally.

Second, compound 49 is disclosed in US 5,668,152 to have higher IC<sub>50</sub> values for the various mechanisms than compound 52 and would therefore reasonably be expected to have a lower apoptotic effect than compound 52. Further, the data presented by Applicant includes different IC<sub>50</sub> values than disclosed in US 5,668,152, such as PKC $\beta$ .1 which Applicant asserts for Example 49 of the prior art as 0.15 $\mu$ M, yet the prior art teaches is 0.03 $\mu$ M. Assuming Applicants data is correct further supports the assertion that the compound of Example 52 would have a much greater apoptotic effect than the compound of Example 49.

Third, Applicants present data based on in vitro assays, which presents unpredictable data. As illustrative of the state of the art, the examiner cites Suggitt and Bibby, *Clinical Cancer Research*, 2005, Vol 11, 971-981. Suggitt and Bibby teaches the unpredictability of treating cancer. Note however, that the current human tumor cell line in vitro screen is generally unpredictable. Modern methods are susceptible to false-

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positive and false-negative results. (page 973 1<sup>st</sup> paragraph on right-hand column).

Difficulty in determining results leads to difficulty in testing for effectiveness of compounds, which leads to unpredictability in treating cancers. Thus, the data does not provide sufficient information with regards to treating prostate cancer in vivo given the unpredictable translation of the evidence to the instantly claimed method.

Fourth, the data presented is not commensurate in scope of the claims. Specifically, only a single compound was tested, but the generic claims allow the R groups to be either H or C1-C4 alkyl. As suggested by Applicants, it is the variation of these groups from compound 49 of the prior art which causes suppression of the AKT pathway, but the data does not present evidence that the various substitutions will have the same effect as compound 52 of the prior art.

### ***Conclusion***

No claims allowed.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

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the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Benjamin Packard whose telephone number is 571-270-3440. The examiner can normally be reached on M-R 8-5 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Frederick Krass can be reached on 571-272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Benjamin Packard/  
Examiner, Art Unit 1612

/Frederick Krass/  
Supervisory Patent Examiner, Art Unit 1612